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Chronic obstructive pulmonary disease, with and without alpha-1-antitrypsin deficiency: management practices in the U.K.

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Alpha-1-antitrypsin deficiency is a common genetic defect associated with the development of severe and rapidly progressive lung disease. This study was undertaken to determine whether respiratory physicians manage patients with alpha-1-antitrypsin (AAT) deficiency differently from patients with chronic obstructive pulmonary disease (COPD) without alpha-1-antitrypsin deficiency. In addition we obtained physicians' views on who should be tested for AAT deficiency.

A questionnaire was administered to 88 respiratory physicians based throughout the U.K. (44 in teaching hospitals). The main outcome measures were pulmonary function tests, radiological assessment, frequency of repeat testing, follow-up and screening protocol for alpha-1-antitrypsin deficiency.

Subjects with homozygous (PiZ) AAT deficiency were more likely to: 1. have baseline and full pulmonary function testing including dynamic flow rates, static lung volumes, and gas transfer; 2. have more comprehensive assessment with high resolution computed tomography (HRCT) thorax and repeated radiological assessment (with annual chest radiography); 3. be followed-up routinely; and 4. have family members tested for alpha-1-antitrypsin deficiency. Testing remains limited for AAT deficiency and is mainly restricted to young patients with COPD.

COPD assessment and management is influenced by the presence of AAT deficiency, which may reflect the poorer prognosis of such patients due to more rapid decline. Assessment and monitoring could be simplified to forced expired manoeuvres, although limited HRCT thorax and tests of gas transfer may prove more sensitive to progression of emphysema. Testing for AAT deficiency in the U.K. remains restricted, which will influence the detection rate for AAT deficiency. A wider policy of testing as advocated by the WHO will detect more patients and also influence our understanding of the natural history of the condition.

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Introduction

Alpha-1-antitrypsin (AAT) deficiency is one of the commonest genetic deficiencies of Caucasians with an incidence as high as one in 1600 in Scandinavia (1). The protein is the major plasma inhibitor of serine proteinases and it is believed to play a critical role in the protection of the lung from proteolytic damage by the enzyme elastase released from activated neutrophils (2). The deficiency was first recognized in 1963 (3) and subsequent studies have confirmed its association with the early development of emphysema and bronchitis (4). Deficient subjects have an increased risk for severe airflow obstruction and have an accelerated decline in lung function, especially if they smoke (5).

In addition to the lung disease, deficient subjects develop neonatal jaundice which may be fatal (6), as well as cirrhosis and primary liver cancer in later life (7).

Although AAT deficiency is relatively common, few of the subjects are identified unless population screening is undertaken (1,8). This is clearly of importance since early identification of the deficiency prior to the establishment of lung disease in particular can lead to a successful modification of lifestyle, especially with respect to smoking habit (9), which will have a major effect upon the long-term health cost burden.

At a recent World Health Organization (WHO) meeting it was highlighted that only 5% of the deficient subjects in the U.K. have been identified by physician testing, as opposed to the predicted number by population screening

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(10). The reasons for this were unknown but may relate to the possibility that most subjects remain reasonably healthy and thus do not present to health-care services. Alternatively, testing could be restricted to the wrong patient population. For instance, the first patients identified (3) were young with marked chronic obstructive pulmonary disease (COPD) and this has generally resulted in continued testing of mainly younger patients. Indeed, recent guidelines on the management of COPD by the European Respiratory Society (ERS) (11) and the British Thoracic Society (BTS) (12) have emphasized testing for young patients. This restricted policy may have led to a predominance of such patients in the American NIH registry of AAT deficiency (13) and continued testing bias.

For these reasons the WHO has recommended much wider testing for AAT deficiency. Furthermore, the WHO has recognized that none of the COPD guidelines published by specialist societies specifically addressed the standards of care required for AAT deficiency.

The purpose of the present study was to determine the current practice of U.K. hospital physicians, with an interest in respiratory disease, in the management of AAT deficiency. In particular we wished to determine whether management was different to that for non-deficient subjects with COPD. Finally we wished to clarify the current policy of the physicians for testing for AAT deficiency in advance of the publication of the BTS guidelines and the WHO report (10).

Methods

We administered a questionnaire (Appendix 1) to 88 consultant respiratory physicians who were based throughout the U.K. and selected at random at a single BTS meeting. Physicians were informed that the questionnaire was to determine how they believed an elderly patient (greater than 50 years of age) with COPD should be managed. Once the answers had been obtained they were asked (with the same questions) if their policy would change if the patient were 50 years of age or less. Finally, they were also asked if patients with the diagnosis of homozygous (PiZ) or heterozygous (PiMZ) AAT deficiency should be managed in the same or a different way. At the end of the questionnaire all physicians were asked who they felt should be tested for AAT deficiency.

The questionnaire inquired into which investigations were routinely undertaken as a baseline to include pulmonary function tests, blood tests (i.e. full blood count and biochemical profile with liver function) and an electrocardiograph. In addition, physicians were asked what further tests they would carry out including an oral steroid trial and inhaled steroid trial (and whether these influenced management), as well as which radiological assessment would be undertaken. Finally, we inquired about the usual frequency of repeat testing for monitoring disease progression as well as the usual follow-up practice for the patient and whether this would be influenced by age or the AAT phenotype.

The questionnaire also inquired about treatment given routinely, including the use of bronchodilators, inhaled steroids and vaccination as well as the use of oral steroids and antibiotics for acute exacerbations as generically defined (a worsening of any symptoms).

Any differences between management policies for individual patient groups were compared by the chi-squared test, or Fisher's test of exact probability when small numbers ($n<5$) were encountered. P-values of less than 0·05 were considered to be statistically significant.

Results

Eighty-eight randomly chosen respiratory physicians (which accounts for 20–25% of the physicians with an interest in respiratory medicine in the U.K.) were questioned at a single BTS meeting. The age of the physicians ranged from 34–65 years and there was an equal representation of teaching and district general hospital physicians. All physicians requested answered the questionnaire.

The routine baseline pulmonary function tests and radiological tests, including annual repeat testing, which U.K. respiratory physicians would routinely carry out are shown in Fig. 1.

SPIROMETRY AND RADIOLOGY

All respiratory physicians felt that all COPD patients should have baseline spirometry and a chest radiograph irrespective of age or AAT phenotype. Fewer physicians arrange full lung function tests (57 or 69%, depending on the age of patient), although 80% would assess lung function fully in PiZ AAT deficient subjects. Serial peak flow monitoring to rule out asthma would be carried out by approximately 40% of physicians, although more (69%) would arrange this if the patient with COPD was young with normal AAT. Eightly-five per cent of physicians would carry out a steroid trial (75% with oral steroids and approximately 10% with inhaled steroids) prior to introducing steroid therapy.

Only 2·3% of physicians would request high resolution computed tomography (HRCT) for patients with a diagnosis of COPD unless they were young (28·4%), or had the PiMZ (13·6%) or PiZ phenotype for AAT deficiency (47·7%).

ANNUAL REVIEW

Few physicians carry out annual lung function testing, although more (35%) would do this for patients with PiZ AAT deficiency. Less than 20% of physicians would arrange for annual repeat chest radiograph unless the patient had PiZ AAT deficiency when a greater number (27·3%) felt this was important.

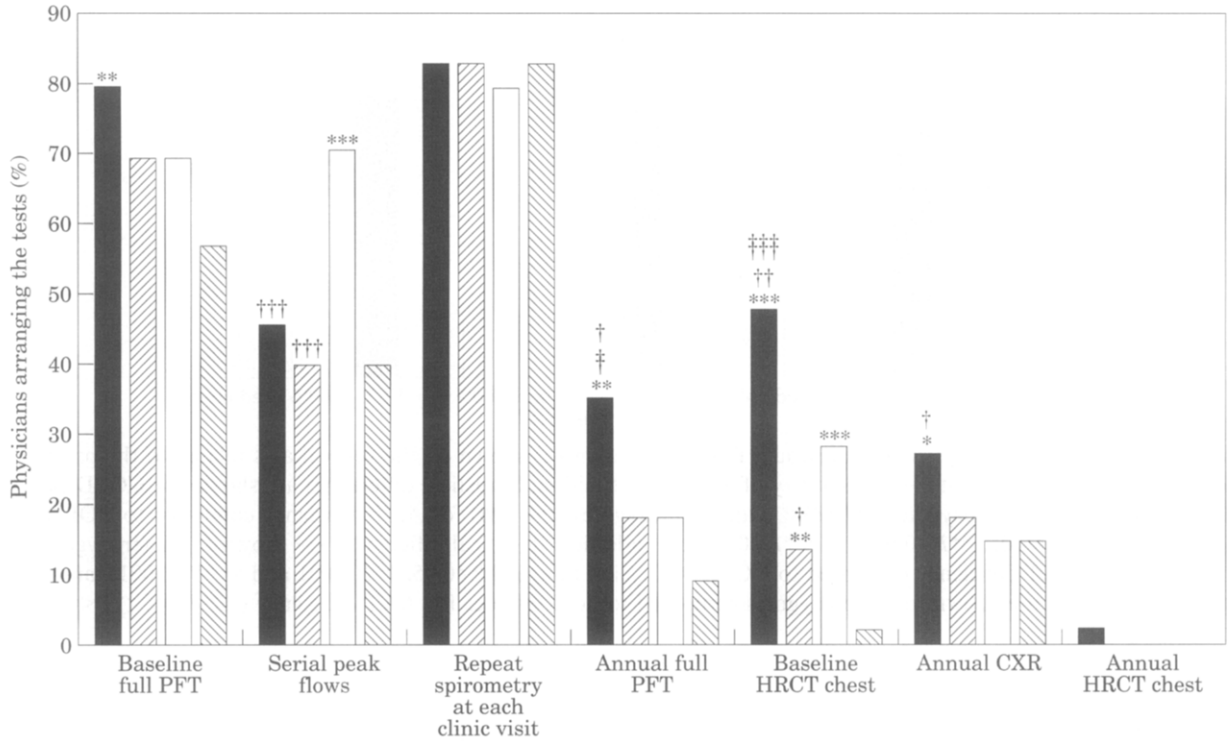

FIG. 1. The percentage of physicians who carry out routine baseline pulmonary function tests and radiological investigations, including annual repeat testing, is shown on the vertical axis for patients with homozygous (PiZ) alpha-1-antitrypsin (AAT) deficiency (■), heterozygous (PiMZ) AAT deficiency (▨), COPD patients <50 years of age (□) and COPD patients >50 years of age (▧). Statistical differences are shown for COPD patients >50 years of age, PiMZ and PiZ for AAT deficiency compared to COPD >50 years of age (*P<0·05, **P<0·01 and ***P<0·001). Statistical differences are also shown for heterozygotes and homozygotes for AAT deficiency compared to COPD <50 years of age (†P<0·05, ††P<0·01 and †††P<0·001). Finally statistical differences are shown for heterozygotes compared to homozygotes for AAT deficiency (‡P<0·05, ‡‡P<0·01 and ‡‡‡P>0·001).

GENERAL INVESTIGATIONS AND MANAGEMENT

In all groups approximately 85% of physicians would arrange a baseline full blood count, approximately 70% a biochemical profile and approximately 55% an electrocardiograph.

A small proportion of physicians (23·9%) would empirically use inhaled steroids over the long term, independent of the results of a steroid trial or pulmonary function reversibility testing. The remainder would use long-term inhaled steroids only if there was a positive steroid trial. Treatment with inhaled bronchodilator therapy was based on the bronchodilator reversibility results by 42% of physicians but of the remainder, 42·1% would use a β_2-agonist agent alone and 11·4% would use combined bronchodilators irrespective of the reversibility testing. Influenza vaccination would be advised annually by 90·9% of physicians and 55·7% would advise pneumovax. Oral steroids and antibiotics would be used routinely by 71·6 and 78·4% of physicians, respectively, for any exacerbation of COPD that led to hospital admission. However if the exacerbation did not require admission, fewer (31·8%) would use oral steroids (P<0·001) but a similar proportion (70·4%) would use antibiotics (P=0·3).

PATIENT FOLLOW-UP

Most physicians (78%) would regularly review patients with PiZ AAT deficiency irrespective of the lung function. However more (90%) would follow-up these patients if the forced expiratory volume in 1 sec (FEV_1) were impaired to less than 50% predicted. Fewer physicians (42% if FEV_1>70% predicted) would review patients who were heterozygous for AAT deficiency and the least (11% if the FEV_1>70% predicted) would review COPD patients over 50 years of age with normal AAT. However, there was again a tendency for a greater number to review each of the patient groups as lung function deteriorated (Fig. 2). The average interval between appointments was similar for each patient group (approximately 7 months; range 1–12 months).

TESTING FOR AAT DEFICIENCY

Most young patients (less than 50 years of age) with COPD would be tested for AAT deficiency by most physicians, whereas this would be infrequently carried out in elderly patients, those with bronchiectasis or patients with other causes of airflow obstruction including asthma. Testing is more likely to be carried out in patients with a family

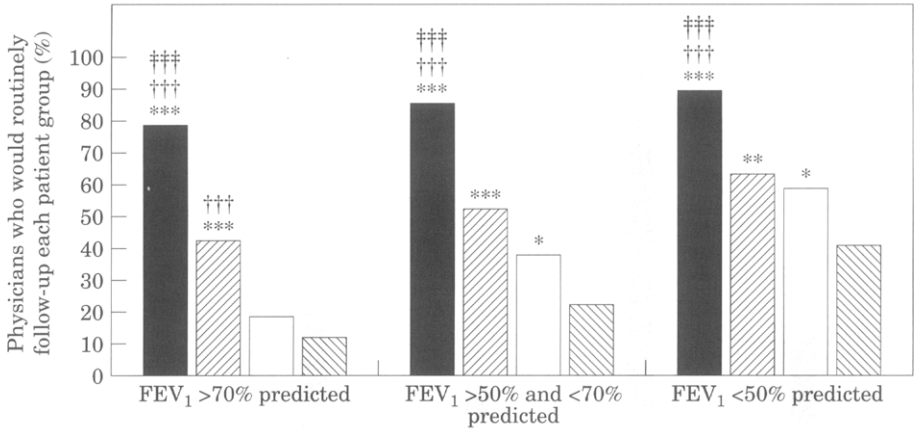

FIG. 2. The percentage of physicians who would follow-up patients is shown on the vertical axis related to the patient subgroup by age, AAT phenotype and severity of airflow obstruction. Statistical differences are shown for COPD patients <50 years of age (□), heterozygotes (PiMZ) (▨) and homozygotes (PiZ) (■) for AAT deficiency compared to COPD >50 years of age (▧) (*P<0·05, **P<0·01 and ***P<0·001). In addition statistical differences are shown for heterozygotes and homozygotes for AAT deficiency compared to COPD <50 years of age (†P<0·05, ††P<0·01 and †††P<0·001), and finally statistical differences are shown for heterozygotes compared to homozygotes for AAT deficiency (‡P<0·05, ‡‡P<0·01 and ‡‡‡P<0·001).

history of chronic lung disease or in family members of a known patient with AAT deficiency. These results are summarized in Table 1.

TEACHING/DISTRICT GENERAL HOSPITAL BASED

The answers to this questionnaire indicated no difference in patient management between consultants who were based in a teaching hospital and those based in a district general hospital (data not shown).

Discussion

This survey has shown that few patients with COPD are tested for AAT deficiency. This practice differs from that recommended by the WHO but the survey preceded publication of the report (10). However, once identified the patients are investigated more extensively and most patients with PiZ AAT deficiency are kept under regular review although there are wide variations in management. Although consensus documents for the management of COPD have been published, the identification and management of patients with AAT deficiency have not been addressed specifically. At present a combined European Respiratory Society and American Thoracic Society Task Force has been established to develop specific guidelines but it will not report until the year 2000. It therefore seems appropriate to assess present views on the management of AAT deficiency and consider their validity in light of current practical and theoretical evidence.

AAT deficiency is common and is associated with several disease conditions. The lung disease is more rapidly progressive in smokers than subjects without deficiency and siblings also have a one in four chance of having deficiency. The pathogenic processes which result in the development and progression of the lung disease have been well defined (2) and this should lead to a different and perhaps more aggressive strategy in management of deficient subjects.

TABLE 1. Current testing practice for AAT deficiency (percentage of physicians who would test subjects in each category)

Young (<50 years) emphysema/COPD	88·6%
Older emphysema/COPD	10·2%
Family history chronic lung disease	44·3%
Patients with bronchiectasis	20·5%
Other airflow obstruction, e.g. bronchiolitis	15·9%
Patients with asthma	2·3%
Family members of PiZ patients	98·9%
Family members of patients who are heterozygous for AAT deficiency	53·4%

BASELINE LUNG FUNCTION TESTING

Optimal clinical practice would indicate that full lung function testing, including dynamic flow rates, static lung volumes and gas transfer, should all be assessed at baseline in order to document fully the physiological status of patients with COPD. The results of the present survey indicate that just over half of the physicians arrange this for COPD patients, although all would carry out dynamic flow rates in line with the BTS guidelines (12). However more (approximately 80%) would obtain full lung function if the patient had AAT deficiency. This did not relate to whether the physician was practicing in a teaching hospital and is likely to reflect the unusual nature of the patient and a wish to document the patient more completely.

SERIAL PEAK FLOWS

Of more interest is the use of serial peak expiratory flow rate (PEFR) monitoring at baseline. This practice enables marked diurnal variation to be identified suggesting a diagnosis of asthma. Significantly more clinicians assess this in young patients with COPD, indicating that asthma is either suspected more frequently in this group or that a different management strategy is believed to be more critical in younger patients who have both a longer life expectancy and may have greater life-style expectations. Surprisingly, PEFR monitoring was no more frequently used to assess patients with AAT deficiency than older COPD patients despite the general belief that such patients present at a young age. This difference in practice probably reflects a conceptional bias that AAT deficient subjects mainly develop fixed airflow obstruction. Studies have, however, shown that many such patients have symptoms suggestive of asthma (14) and reversible airflow obstruction (15). Indeed a recent study highlighted that lung function deterioration occurs in middle-aged non-smokers with AAT deficiency who have a history of wheezing (14). It would therefore seem appropriate to assess variability of airflow obstruction in all subjects with AAT deficiency and, where indicated, to treat appropriately.

DISEASE MONITORING

All physicians felt that an initial chest X-ray should be performed in all patients with COPD, even though this would not help in the assessment or diagnosis of generalized emphysema. It is likely that this is performed as a screening test for incidental lung lesions or possibly for identification of localized bullous disease as advocated in the guidelines (12). HRCT scan, however, has now become the best method for assessing the presence, extent and progression of emphysema, proving more effective than lung function testing (16,17). Despite this, HRCT is rarely performed although almost half the physicians felt that it should be performed in AAT deficiency. Recent studies, however, have indicated that limited HRCT (with appropriate reduction in radiation dosage) provides a sensitive assessment of progression of emphysema in AAT deficiency (17). Despite this observation few physicians repeat the test, whereas chest X-rays, which are poorly sensitive, are repeated by one-third of physicians.

On the other hand, full lung function is repeated annually in AAT deficiency by over one-third of all physicians. Current epidemiological data on progression of lung disease are related to FEV_1 measurements alone which are simple (and hence cost-effective) and may reflect prognosis and hence referral for transplantation. However, tests of gas transfer are a more specific measure of the presence of emphysema and clearly relate to the changes on CT scan (18). It therefore remains possible that these more specific tests (though more expensive) may provide a clearer measure of progression. Clearly, further studies of the use of these tests in disease monitoring are indicated although preliminary data from our registry indicate that both HRCT and carbon monoxide transfer coefficient (KCO) (19) show significant changes over 12 months.

The extent of disease monitoring should depend on the phenotype, smoking status and whether the patients have lung disease or not. Disease monitoring is of importance in determining prognosis in PiZ AAT deficient individuals with lung disease and annual follow-up is probably indicated and should, at present, include FEV_1 (which may decline exponentially). In addition PiZ AAT deficient individuals without lung disease should undergo periodic monitoring (for example every 2–3 years), even for non-smokers, as lung disease may develop later in life (14). Furthermore, such information will be critical in the understanding of the natural history of the deficiency.

Heterozygote subjects are not thought to be at increased risk for the development of COPD. Thus at present it seems reasonable to monitor such patients in a similar way to non-deficient COPD patients. In the absence of lung disease (asymptomatic siblings) monitoring seems inappropriate except for research purposes. However, it is probably reasonable to check the phenotype of any spouse or partner to determine the risks of deficiency (PiZ) in any children.

OTHER TESTS

Of the other baseline investigations it is worth noting that only 70% of physicians perform blood tests that include liver function, even in subjects with AAT deficiency who are particularly susceptible to the development of cirrhosis and primary liver cancer (7). This may reflect a lack of awareness, the reduced tendency for lung and liver disease to co-exist (20) or a belief that the liver diseases cannot be influenced. Whereas this may be pathologically correct, alcohol avoidance and dietary modification can stabilize liver function thereby delaying the progression of liver failure leading to the need for transplantation. However, close monitoring in subjects with cirrhosis is necessary to identify hepatoma at an early stage when surgery may be possible.

MANAGEMENT

In general, patients with AAT deficiency are managed in the same way as other patients with COPD. Particular notice should be drawn to the use of inhaled steroids and antibiotics. The progression of disease in the presence of AAT deficiency is believed to be more rapid and dependent on tissue destruction or damage in close proximity to the migrating and activated neutrophil (2). The low concentration of AAT in the deficient subjects fails to control the area of connective tissue degradation by neutrophil enzymes adequately (21), leading to more extensive damage. Thus it would appear to be important to treat episodes of acute exacerbations associated with increased neutrophil influx both rapidly and effectively. In addition neutrophil traffic should, if possible, be modified even in the stable clinical state (2). With this in mind the use of inhaled steroids could be recommended empirically in these patients at present since such treatment has been shown to reduce

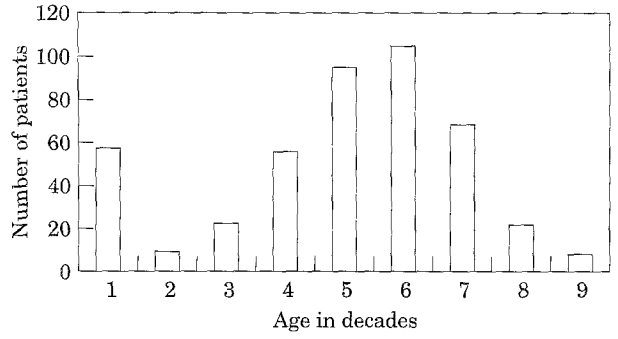

FIG. 3. The age range of patients identified as PiZ individuals by the Protein Reference laboratory in Sheffield between 1995 and 1997 is shown. The vertical axis indicates the number identified in each decade of life.

the chemotactic activity of airways secretions and increase the neutrophil elastase inhibitory capacity (22), both of which might be expected to reduce lung damage (2). Confirmation of the long-term efficacy of such an approach clearly requires a controlled trial; however, as almost 25% of physicians already use such therapy empirically in COPD it seems reasonable to adopt this approach in AAT deficiency where the theoretical arguments for their use are stronger.

Replacement therapy is theoretically even more likely to be beneficial by limiting the radius of lung damage caused by migrating neutrophils (21). Indeed, the recent NIH survey provides tantalizing evidence that replacement therapy may influence both FEV_1 decline in a subset of patients with moderate impairment as well as overall mortality (23). Unfortunately this was not a controlled trial, the non-treated patients were not well matched and treated patients would have been exposed to more health-care workers because of their weekly infusions. Clearly a controlled trial is urgently required to determine the efficacy and need for replacement therapy.

AAT TESTING

The attitudes to testing for AAT deficiency are worthy of specific comment. There remains a general belief amongst respiratory physicians and those surveyed here that testing should be generally limited to young people with COPD or those with a strong family history. This is in keeping with the recent recommendations by the (BTS) (12). However, it has long been known that bronchiectasis is present pathologically (24) and is regularly seen on CT scans (25) of patients with deficiency. In addition, recent studies (14,15,26) have highlighted the presence of asthma or asthmatic symptoms in deficient subjects. Finally, it is known that the diagnosis can even be made in old age. Indeed, the age range of subjects identified over the past 3 years at the protein reference laboratory in Sheffield is clearly wide (Fig. 3) and the peak age is the sixth decade. It therefore seems appropriate to emphasize the current WHO guidelines that all patients with COPD, all adult asthmatics and all patients with bronchiectasis should be tested (10). In addition, testing families of AAT deficient subjects (bot PiMZ and PiZ) will detect other deficient subjects an provide information necessary for appropriate geneti counselling.

Although it could be argued that identification of mor elderly patients with AAT deficiency may not influenc their subsequent management, it should be remembere that such subjects have increased mortality and, in particu lar, other family members at risk. Indeed, non-index case are more likely to have better preserved lung function (27 and hence will benefit more from the best clinical practice Ultimately the aim would be to identify young family members who can successfully be advised against starting smoking (9), thereby providing a long-term benefit to both themselves and the health-care services.

Conclusion

At present it seems appropriate to assess all AAT deficient subjects as fully as possible and advise them about family screening and lifestyle. Follow-up assessment should probably be limited to forced expiratory manoeuvres at present with vital capacity although the role of limited HRCT and tests of gas transfer should be explored. Testing should be performed (initially) on an annual basis (except in heterozygotes with normal lungs, as such patients are unlikely to benefit from follow-up) until it is clear that progression is not rapid when a reduction in frequency of assessment can be instigated. All patients should be under the care of physicians with an interest in this deficiency and documented on a national registry. A registry will be of major importance for learning more about the natural history of the disease and in particular why only a portion are susceptible to the liver or lung manifestation. In addition a registry will provide the core information critical for the design and implementation of careful intervention studies. At present, a U.K. registry has been established with information on over 200 patients. An international committee of 12 national registries has been established with a common database in Sweden, which makes the likelihood of controlled trials a realistic option.

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Appendix A

Consultant _____

Hospital _____

City _____

Country _____

Teaching/DGH _____

Date questionnaire _____

INVESTIGATION AND MANAGEMENT OF COPD

If a patient presents as an in-patient or in your clinic as COPD

Tick and indicate how often you would repeat the tests, e.g. 6-monthly, mark 6; yearly, mark 12 etc.

1. Lung function

	Age >50			Age <50		
	Yes	No	Repeat	Yes	No	Repeat
Basic spirometry	☐	☐	☐	☐	☐	☐
Flow volume curves	☐	☐	☐	☐	☐	☐
Static lung volumes	☐	☐	☐	☐	☐	☐
Gas transfer factor	☐	☐	☐	☐	☐	☐
Reversibility β_2-agonist (if indicated)	☐	☐	☐	☐	☐	☐
Reversibility anticholinergic	☐	☐	☐	☐	☐	☐
Reversibility to both on separate days	☐	☐	☐	☐	☐	☐
Serial peak flows	☐	☐	☐	☐	☐	☐

2. Diagnostic tests

	Age >50			Age <50		
	Yes	No	Repeat	Yes	No	Repeat
Full blood count	☐	☐	☐	☐	☐	☐
ESR/plasma viscosity	☐	☐	☐	☐	☐	☐
Biochemistry profile	☐	☐	☐	☐	☐	☐
Thyroid function	☐	☐	☐	☐	☐	☐
Immunoglobulins	☐	☐	☐	☐	☐	☐
Auto-antibodies	☐	☐	☐	☐	☐	☐
Complement	☐	☐	☐	☐	☐	☐
Cilia studies	☐	☐	☐	☐	☐	☐
Sweat tests	☐	☐	☐	☐	☐	☐

3. Radiology

	Age >50			Age <50		
	Yes	No	Repeat	Yes	No	Repeat
PA CXR	☐	☐	☐	☐	☐	☐
Left lateral CXR	☐	☐	☐	☐	☐	☐
CT chest	☐	☐	☐	☐	☐	☐
if Yes, is it a HRCT?	☐	☐		☐	☐	
is it in inspiration and expiration?	☐	☐		☐	☐	
MRI chest	☐	☐	☐	☐	☐	☐

4. Further tests

	Age >50		Age <50	
	Yes	No	Yes	No
Formal oral steroid trial	☐	☐	☐	☐
Inhaled steroid trial	☐	☐	☐	☐
ECG	☐	☐	☐	☐
Exercise tests	☐	☐	☐	☐

5. Treatment – which bronchodilator do you routinely use first?

	Age >50		Age <50	
	Yes	No	Yes	No
β_2-agonist first	☐	☐	☐	☐
Anticholinergic first	☐	☐	☐	☐
Combination first	☐	☐	☐	☐
Based on bronchodilator studies	☐	☐	☐	☐
Theophylline	☐	☐	☐	☐
Inhaled steroids empirically	☐	☐	☐	☐
Inhaled steroids based on steroid trial	☐	☐	☐	☐
Advise yearly flu vaccinations	☐	☐	☐	☐
Advise pneumovax	☐	☐	☐	☐

6. Treatment continued

	Age >50		Age <50	
	Yes	No	Yes	No
As out-patient use oral steroids for all exacerbations	☐	☐	☐	☐
As out-patient use antibiotics for all exacerbations	☐	☐	☐	☐
As in-patient use oral steroids for all exacerbations	☐	☐	☐	☐
As in-patient use antibiotics for all exacerbations	☐	☐	☐	☐

7. Medical follow-up arrangements

	Age >50		Age <50	
	Yes	No	Yes	No
Patients on home nebulised bronchodilators	☐	☐	☐	☐
If Yes, when do you see them?	_____ months			
Patients on LTOT	☐	☐	☐	☐
If Yes, when do you see them?	_____ months			
Patients with severe airflow obstruction not yet needing home neb. bronchodilators or LTOT (FEV_1 <35% predicted)	☐	☐	☐	☐
If Yes, when do you see them?	_____ months			
Patients with moderate airflow obstruction FEV_1 35–60% predicted)	☐	☐	☐	☐
If Yes, when do you see them?	_____ months			
Patients with mild airflow obstruction (FEV_1 >60% predicted)	☐	☐	☐	☐
If Yes, when do you see them?	_____ months			
All emergency admissions?	☐	☐	☐	☐
If Yes, when do you see them?	_____ months			

INVESTIGATION AND MANAGEMENT OF a_1AT DEFICIENCY

Homozygous (PiZ) and heterozygous (MZ)

Tick and indicate how often you would repeat the tests, e.g. 6-monthly, mark 6; yearly, mark 12 etc.

1. Lung function

	PiZ			PiMZ		
	Yes	No	Repeat	Yes	No	Repeat
Basic spirometry	☐	☐	☐	☐	☐	☐
Flow volume curves	☐	☐	☐	☐	☐	☐
Static lung volumes	☐	☐	☐	☐	☐	☐
Gas transfer factor	☐	☐	☐	☐	☐	☐
Reversibility β_2-agonist (if indicated)	☐	☐	☐	☐	☐	☐
Reversibility anticholinergic	☐	☐	☐	☐	☐	☐
Reversibility to both on separate days	☐	☐	☐	☐	☐	☐
Serial peak flows	☐	☐	☐	☐	☐	☐

2. Diagnostic tests

	PiZ			PiMZ		
	Yes	No	Repeat	Yes	No	Repeat
Full blood count	☐	☐	☐	☐	☐	☐
ESR/plasma viscosity	☐	☐	☐	☐	☐	☐
Biochemistry profile	☐	☐	☐	☐	☐	☐
Thyroid function	☐	☐	☐	☐	☐	☐
Immunoglobulins	☐	☐	☐	☐	☐	☐
Auto-antibodies	☐	☐	☐	☐	☐	☐
Complement	☐	☐	☐	☐	☐	☐
Cilia studies	☐	☐	☐	☐	☐	☐
Sweat tests	☐	☐	☐	☐	☐	☐

3. Radiology

	PiZ			PiMZ		
	Yes	No	Repeat	Yes	No	Repea
PA CXR	☐	☐	☐	☐	☐	☐
Left lateral CXR	☐	☐	☐	☐	☐	☐
CT Chest	☐	☐	☐	☐	☐	☐
if Yes, is it a HRCT?	☐	☐		☐	☐	
is it in inspiration and expiration?	☐	☐		☐	☐	
MRI chest	☐	☐	☐	☐	☐	☐

4. Further tests

	PiZ		PiMZ	
	Yes	No	Yes	No
Formal oral steroid trial	☐	☐	☐	☐
Inhaled steroid trial	☐	☐	☐	☐
ECG	☐	☐	☐	☐
Exercise tests	☐	☐	☐	☐

5. Treatment—which bronchodilator do you routinely use first?

	PiZ		PiMZ	
	Yes	No	Yes	No
β_2-agonist first	☐	☐	☐	☐
Anticholinergic first	☐	☐	☐	☐
Combination first	☐	☐	☐	☐
Based on bronchodilator studies	☐	☐	☐	☐
Theophylline	☐	☐	☐	☐
Inhaled steroids empirically	☐	☐	☐	☐
Inhaled steroids based on steroid trial	☐	☐	☐	☐
Advise yearly flu vaccinations	☐	☐	☐	☐
Advise pneumovax	☐	☐	☐	☐

6. Treatment continued

	PiZ		PiMZ	
	Yes	No	Yes	No
As outpatient use oral steroids for all exacerbations	☐	☐	☐	☐
As outpatient use antibiotics for all exacerbations	☐	☐	☐	☐
As inpatient use oral steroids for all exacerbations	☐	☐	☐	☐
As inpatient use antibiotics for all exacerbations	☐	☐	☐	☐

7. Medical follow-up

	PiZ		PiMZ	
	Yes	No	Yes	No
Regular follow up?	☐	☐	☐	☐
If Yes, how often do you see them?	_____		_____ months	

8. Would you carry out family studies?

	Yes	No
PiZ α_1AT deficient patients	☐	☐
PiMZ α_1AT deficient patients	☐	☐

9. Would you screen the following for α_1AT deficiency?

	Yes	No
COPD <50 years	☐	☐
All COPD	☐	☐
Family history of chronic lung disease	☐	☐
Asthma	☐	☐
Bronchiectasis	☐	☐
Other airflow obstruction (bronchiolitis etc.)	☐	☐